Since the development of coronary angioplasty in the late 1970s, there have been a series of technical advancements that have improved the outcome of the procedure. Clearly, the biggest advance was to move from balloon angioplasty to intracoronary stenting and now to drug-eluting stents (DES). These advances have been shown to reduce in-hospital events and to dramatically lower the incidence of restenosis, the long-standing “Achilles’ Heel” of percutaneous coronary intervention (PCI). As these advances have occurred, there has been concern about the ability of society to afford these new therapies.

What we seek in medical care is value; that is, good medical care that is worth what we pay for it. This may be evaluated for a particular new service, whether diagnostic or therapeutic, by performing a cost-effectiveness evaluation. Healthcare economics has grown as a field in recent years, and there are now published standards for cost-effectiveness evaluations. The cost-effectiveness of a new procedure is best expressed in cost per quality adjusted life year (QALY) gained. More recently, economic studies have been conducted as part of randomized controlled trials. This offers the ability to both get patient level as opposed to summary data and also to benefit from a randomized comparison. Economic evaluations benefit from the lack of selection bias in randomized trials just as much as clinical comparisons do.

A model economic evaluation performed as part of the randomized trial of DES, the Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients With De Novo Native Coronary Artery Lesions (SIRIUS) trial, is offered in the current issue of Circulation by Cohen et al. In the SIRIUS trial, 1058 patients undergoing elective coronary stent implantation were randomized to a bare metal stent or the sirolimus DES. The patients were then followed up for 1 year. The sirolimus stent reduced the restenosis rate by 75% from 36.3% to 8.9%, and reduced the rate of repeat revascularization from 28.4% to 13.3%. No significant advantage was found with regard to death or myocardial infarction. This is consistent with data that show that restenosis results in recurrent angina and the need for repeat revascularization, but rarely causes cardiovascular events. Initial hospital costs were higher in the sirolimus stent arm ($11 345 versus $8464; P<0.001), entirely because of the difference in cost between the stents ($2900 versus $900). However, because there were fewer repeat revascularizations, the follow-up costs were lower in the sirolimus stent arm. Thus, at 1 year, there was little difference in cost, at $16 813 with the sirolimus DES and $16 504 with bare metal (P=0.64). This gives a cost difference of $309 (95% confidence interval $977 to $1594).

The cost-effectiveness was expressed in cost per repeat revascularization avoided and cost per QALY gained. Bootstrap analysis of both cost and outcome was used to consider the conjoint variance of these measures. This permits the calculation of the percent of estimates where the DES offered better outcome at lower cost (DES dominant) and the percent of estimates where the DES offered better outcome than some benchmark. The incremental cost-effectiveness ratio (ICER) in cost per repeat revascularization avoided using baseline assumptions was $1650, with 98% of estimates less than $10 000 per repeat revascularization avoided. The ICER in cost per QALY gained was $27 540, with 63% of estimates less than $50 000 per QALY gained.

DES require 3 months of platelet adenosine diphosphate blockade with clopidogrel because of concern over increased incidence of subacute thrombosis, compared with the standard 1 month with bare metal stents. Thus, the base case assumed that patients would get 1 month of clopidogrel with the bare metal stent and 3 months of clopidogrel with the DES. However, given the results of the Percutaneous Coronary Intervention-Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (PCI CURE) and Clopidogrel for Reduction of Events During Observation (CREDO) trials, which showed benefit of continuing clopidogrel for up to a year, there may little difference in clopidogrel use between patients with and without DES. In addition, if longer DES were available, fewer stents might have been needed. If there were no difference in clopidogrel usage and longer stents became available, then there would be a point estimate to cost savings with the DES, a delta of $44 (95% confidence interval $1325 to $1239), and the point estimate would be for DES to be a dominant strategy, lowering cost and improving outcome. However, this must be considered a secondary or sensitivity analysis. The base case presented above ($1650 per event averted and $27 540 per QALY gained) remains the most grounded in data.

The analyses that led to these results are elegant and quite definitely state-of-the-art for cost-effectiveness analysis. However, there are some concerning issues that are worthy of discussion. As noted, restenosis rarely results in death or myocardial infarction. It does result in recurrent symptoms...
of angina, often leading to repeat revascularization. Indeed, in the SIRIUS trial, the DES arm did not have a lower rate of death or myocardial infarction than the bare metal stent arm.\(^5\) Thus, the efficacy of the DES is based on avoiding recurrent angina and avoiding additional revascularization procedures. Thus, DES improve quality of life and have the potential to decrease cost. Clearly, restenosis that causes angina decreases quality of life. Undergoing repeat revascularization is unpleasant and will decrease quality of life, albeit rather briefly. Dr Cohen and colleagues\(^5\) argue that society has shown a willingness to pay up to $10,000 to avoid repeat revascularization, and the point estimate of $1650 certainly seems reasonable. However, these are rules of thumb and may be adequate to help inform policy makers, but they are probably not sufficient to influence public policy.

Reevaluating the data in cost per QALY gained would appear to place the authors of firmer ground. This is because this metric can be used in cost-effectiveness analyses from all disciplines and published standards exist.\(^3\) The familiar metric of cost per QALY gained will be well known to policy makers and payers and can more certainly help inform decision-making. That being said, the common benchmark of $50,000 per QALY gained reflects public policy rather than any scientifically valid threshold.

There are limitations to the present analysis in cost per QALY gained. The DES did not prevent death or events, i.e., myocardial infarction, that could lead to an earlier death at some time in the future. Thus, there were no life years gained with the DES. How, then, were QALYs gained? This is entirely related to improved quality of life, in this case measured with utility.\(^1\) Utility is an overall measure of health status, which measures the patient’s preference for perfect health compared with his or her present health state. It is generally scaled from zero to one, with zero being the utility of death and one being the utility of perfect health. Utility was not measured in the SIRIUS trial; rather, the authors\(^5\) estimated utility from the measure of utility in the Stent Primary Angioplasty for Myocardial Infarction (Stent-PAMI) trial, utilizing a utility for 1 year without repeat revascularization of 0.86 and for 1 year with repeat revascularization of 0.80.\(^1\) Utility in Stent-PAMI was measured with a survey called the EQ-5D.\(^13\) Although often used, it is probably not as accurate a measure of utility as direct patient preference measures that require the patient to actively consider how much life they would give up or what risk of death they would take to achieve perfect health. Utility values with surveys are probably lower than with patient preference measures. In addition, the Stent-PAMI population was somewhat different from the current one,\(^5\) being composed of people who had suffered an acute myocardial infarction. Finally, utility will change over time, and it is not clear that the dip in utility for patients undergoing repeat revascularization was adequately reflected in Stent-PAMI.\(^14\) All these arguments may seem to be quibbling, but if there is no difference in survival or events that will be reflected in survival, then accurate measurement of utility is critical. These problems add uncertainty to the measure of utility, which would not be reflected in the variance accounted for by the bootstrap analysis.

What is certain is that repeat revascularization is expensive, and here there is considerable potential, perhaps not currently realized, for DES to actually save money. The sensitivity analyses, which Cohen et al\(^5\) offer, suggest that DES could potentially save money. However, there is far greater potential for this as the technology for making DES improves or competitors enter the market place and drive down the price.

Are DES going to be cost-effective in all populations? The generalizability of cost-effectiveness analyses based on clinical trials needs to be considered in much the same way that the clinical results are considered. Subgroup analysis by Cohen et al\(^5\) suggest that the DES was dominant in patients with smaller vessels and longer lesions. In contrast, the DES was of more marginal cost-effectiveness in vessels with reference diameters over 3 mm. Large databases, such as the American College of Cardiology National Cardiovascular Data Registry (ACC/NCDR), may help inform us about efficacy, and if not directly cost, at least resource utilization more widely for DES.\(^15,16\)

As pointed out by Cohen et al,\(^5\) their analysis is presented from a societal point of view. Although this is proper analytically, it does not represent the economic impact of DES from the perspective of other stakeholders in the healthcare system. In particular, hospitals may be adversely affected by DES.\(^17,18\) Although new diagnosis-related groups (DRGs) for DES with (DRG 526) and without (DRG 527) acute myocardial infarction have been created by the Centers for Medicare and Medicaid Services, these DRGs may not be sufficient to cover the acquisition costs of the DES compared with the DRGs for bare metal stents (DRGs 516 and 517). In addition, hospitals will be adversely affected because of the reduced incidence of repeat revascularization and the potential loss of patients going to cardiac surgery if more patients have stents placed instead. On the other hand, and although DES are not likely to change the overall guideline-based indications for revascularization, physicians may be inclined to place stents in patients who they would otherwise have treated medically in the absence DES. The adverse effect on hospitals will also be mitigated as the cost falls with improved manufacturing techniques and increasing competition.

The major winner would appear to be the device companies, which will have potential windfall profits. However, the cost of manufacture may be substantial and the cost of development was certainly considerable. The real winners are patients who will have better outcomes with improved stents.

Finally, improved technical PCI with DES does not lesson the need to meet other patient needs, including equitable access, PCI in patients who meet guidelines, safe and effective PCI, and documentation by participating in registries such as the ACC/NCDR. Finally, it goes without saying that PCI with DES is not a cure for coronary disease and will not prevent progression of atherosclerosis, and as such, the focus in follow-up on risk factor control remains as important as ever. Secondary risk factor control is cost-effective too.\(^14,19\)

References


**Key Words:** Editorials • stents • drugs
Economics of Sirolimus-Eluting Stents: Drug-Eluting Stents Have Really Arrived
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Circulation. 2004;110:472-474
doi: 10.1161/01.CIR.0000136820.77558.B1
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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